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Book Reviews

Dynamics of Proteins and Nucleic Acids

By J.A. McCammon and S.C. Harvey

Cambridge University Press; Cambridge, 1988

xii + 234 pages. £11.95, $19.95

This short, but concise, description of the methods of molecular dynamics (MD) applied to biomacromolecules was prepared by two well-known pioneers, indeed amongst the initiators, of the application of the methods of statistical physics to molecular biology.

The complexity of macromolecules in biological systems is a challenging problem. X-ray (and neutron) diffraction and NMR spectroscopy continue to furnish invaluable data on the fine structure of many proteins, nucleic acids and, more recently, model oligonucleotides, as well as their interactions with various ligands, e.g. enzyme-inhibitor and oligonucleotide-intercalator complexes.

The data derived from X-ray structures have, in turn, made possible further refinements with the aid of theoretical approaches, such as the use of the Monte Carlo method to predict the hydration of a mini-helix of B-DNA, subsequently confirmed by a crystallographic study. But even these theoretical methods are limited to a description of the properties of molecules largely from a *static* viewpoint. The concept that structural fluctuations occur in macromolecules, and that these are intimately related to biological function, is by no means new, and is reflected in frequent references to protein 'mobility' and the 'breathing' of a double helix.

What is now novel and fascinating is the extension of the theoretical methods to include *time-dependence*, e.g. changes in conformation accompanying ligand-receptor interactions, in other words the dynamics of the molecular processes leading to an 'induced fit', also referred to as 'docking'. Such calculations by means of molecular dynamics are based on a combination of methods of classical molecular mechanics and statistical physics for describing the fluctuations of many-body systems.

The volume presents a reasonably good description of the fundamental structures of proteins and nucleic acids, and the biochemical processes they participate in. This is followed by an outline of the various techniques of computer simulation and statistical mechanics employed in the calculations. Extensive descriptions are presented of the type of information gleaned during the past 10 years with the use of MD methods to study biomacromolecules and, in some instances, comparisons with experimental results, such as those obtained by means of dynamic NMR spectroscopy.

A rather brief section describes potential practical future developments in terms of computing techniques and the methodology employed, including possible extension of the time scale of the processes investigated from subnanoseconds to microseconds, or even longer. Highly relevant to this are current new developments in the technique of millisecond crystallography (Laue diffraction) to follow experimentally the changes in conformation of a protein during a reaction (see Ringe, D. (1987) Nature, Sept.10, page 102, and references cited).

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